UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte ERIC N. OLSON, STEPHEN R. GRANT, and JEFFREY D. MOLKENTIN

Appeal No. 2005-2238
Application No. 09/061,417

ON BRIEF[1]

Before ELLIS, ADAMS, and GREEN, Administrative Patent Judges.

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1, 4 and 9, which are all the claims pending in the application.

Claims 1, 4 and 9 are reproduced below:

1. A method of treating hypertrophy in a subject comprising the step of inhibiting the function of NF-AT3 in a cardiomyocyte, wherein the inhibition of NF-AT3 function inhibits hypertrophic gene expression, thereby treating hypertrophy.

4. The method of claim 1, wherein inhibiting the function of NF-AT3 comprises contacting said cardiomyocyte with an agent that binds to and inactivates NF-AT3.

[1] Appellants waived (Paper received August 22, 2005) their request for oral hearing.

9. The method of claim 4, wherein the agent that binds to and inactivates NF-AT3 is an antibody preparation or a small molecule inhibitor.

The references relied upon by the examiner are:

Reid, et al. (Reid), "Determinants of left ventricular function one year after cardiac transplantation," Br. Heart J., Vol. 59, pp. 397-402 (1988)

McCaffrey, et al. (McCaffery), "Isolation of the Cyclosporin-Sensitive T cell Transcription Factor NFATp," Science, Vol. 262, pp. 750-754 (1993)

Haverich et al. (Haverich) "Cyclosporin A and Transplant Coronary Disease After Heart Transplantation: Facts and Fiction," Transplantation Proceedings, Vol. 26, No. 5, pp. 2713-2715 (1994)

Crystal, "Transfer of Genes to Humans: Early Lessons and Obstacles to Success," Science, Vol. 270, pp. 404-410 (1995)

Gura, "Antisense Has Growing Pains," Science, Vol. 270, pp. 575-577 (1995)

Miller, et al. (Miller), "Targeted vectors for gene therapy," FASEB J., Vol. 9, pp. 190-199 (1995)

Martínez-Martínez et al. (Martínez-Martínez), "Blockade of T-Cell Activation by Dithiocarbamates Involves Novel Mechanisms of Inhibition of Nuclear Factor of Activated T Cells," Molecular and Cellular Biology, Vol. 17, No. 11, pp. 6437-6447 (1997)

Verma et al. (Verma), "Gene therapy-promises, problems and prospects," Nature, Vol. 389, pp. 239-242 (1997)

Deonarain, "'Ligand-targeted receptor-mediated vectors for gene deliver," Exp. Opin. Ther. Patents, Vol. 8, No. 1, pp. 53-69 (1998)

GROUNDS OF REJECTION

Claims 1, 4 and 9 stand rejected under 35 U.S.C. § 112, first paragraph, as being based on a specification that fails to adequately describe the claimed invention.

Claims 1, 4 and 9 stand rejected under 35 U.S.C. § 112, first paragraph, as being based on an insufficient disclosure to support or enable the scope of the claimed invention.

Claim 1 stands rejected under 35 U.S.C. § 102(b) as anticipated by Haverich or Reid.

We affirm the rejection of claims 1, 4 and 9 under the written description provision of 35 U.S.C. § 112, first paragraph. Having disposed of all claims under the written description provision, we do not reach the rejection of the same claims under the enablement provision of 35 U.S.C. § 112, first paragraph. We reverse the rejection under 35 U.S.C. § 102(b).

DISCUSSION

Written Description:

Claims 1, 4 and 9 stand rejected under the written description provision of 35 U.S.C. § 112, first paragraph. According to appellants (Brief, page 3), "[t]he claims stand or fall together." Since all claims stand or fall together, we limit our discussion to representative independent claim 1. Claims 4 and 9 will stand or fall together with claim 1. In re Young, 927 F.2d 588, 590, 18 USPQ2d 1089, 1091 (Fed. Cir. 1991).

As we understand the examiner's argument (Answer, pages 5-7), appellants' claimed invention is open to inhibiting the function of NF-AT3 in a

cardiomyocyte by any means. In this regard, the examiner finds (Answer, pages 5-6), appellants'

> specification discloses that [the] agent that reduces the expression of NF-AT3 could be an antisense construct or an antibody or a small molecule inhibitor[2].... The specification also contemplates the use of a mimetic of beta-turns within GATA4[3], that binds to NF-AT3... [and] two calcineurin inhibitors, cyclosporin A, and FK506....

However, the examiner finds (Answer, pages 6-7), the specification only provides written descriptive support for (1) a single chain antibody antagonist of NF-AT3, (2) cyclosporin A, and (3) FK506, of which the latter two do not bind[4] to NF-AT3.

In addition, the examiner finds (Answer, page 7), "no three dimensional structure of GATA4 or NF-AT3 is disclosed in the specification, nor in the art." In this regard, the examiner finds that in University of Rochester v. G.D. Searle, 358 F.3d 916, 925, 69 USPQ2d 1886, 1894 (Fed. Cir. 2004), the court held "even with the three-dimensional structures of enzymes ... in hand, it may even now not be within the ordinary skill in the art to predict what compounds might bind to and inhibit them...." Accordingly, the examiner asserts (id.), "[t]here is no suggestion in the specification of how such NF-AT3 inhibitor compounds could be made or otherwise obtained other than by trial-and-error."

In response, appellants assert (Brief, page 6) that their specification provides "specific examples and specific molecules ... so that one of skill in the

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[2] See e.g., claim 9 with depends ultimately from, and further limits the "agent" of claim 1 to an antibody preparation or a small molecule inhibitor.

[3] According to appellants (Brief, page 7), the Gorczynski declaration confirms that "those of skill in the art would not doubt that GATA4 does indeed bind to NF-AT3...."

[4] We note that claims 4 and 9 depend ultimately from claim 1 and require that the agent which inhibits the function of NF-AT3 "binds to and inactivates NF-AT3."

art would be able to visualize or recognize the subject matter of the claims." According to appellants (Brief, page 7), unlike the facts in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997), "where the DNA molecules at issue had not yet been discovered, a number of the NF-AT3 targeting molecules disclosed by appellants are already known, and thus have been sufficiently described to put the public in possession of the invention."

In response, the examiner finds (Answer, page 8), appellants' limited disclosure of a single chain antibody against NF-AT3, cyclosporin A and FK506 is not considered to "be a representative number of species of small molecule inhibitors that bind to and inactivate ... NF-AT3" as required by appellants' claimed invention. Further, the examiner disagrees with appellants' assertion (Brief, page 8) that their "specification goes beyond simply claiming an undescribed molecule, it actually refers to GATA4 mimetics, DTC's, antisense molecules (p. 27, lines 12-20), antibodies, competitive inhibitors of NF-AT3 (p. 30, line 21) as well as other proteins that inhibit NF-AT3...." We find, however, that contrary to appellants' assertion, page 27, lines 12-20 of appellants' specification does not refer to GATA4 mimetics, or DTC's.

The examiner recognizes, however, that appellants' "specification contemplates the use of mimetics of beta-turns within GATA4, that bind[s] to NF-AT3 in a manner analogous to the transcriptional factor GATA4, and specifically inhibits NF-AT3 binding to GATA4...." Answer, page 23. The examiner finds, however, that the specification does not disclose the structure of any GATA4 mimetics. Id. Further, the examiner finds (Answer, bridging paragraph, pages

23-24), "although the structure of NF-AT3 is known in the art ... the structure of numerous other competitive inhibitors of NF-AT3..., as well as numerous peptides that bind to and inactivate NF-AT3 is [sic] not disclosed in the specification." the particular small antisense molecules that inhibit in vivo function of NF-AT3 is not disclosed in the specification. In this regard, we note that appellants' specification discloses (page 28), "[w]ith respect to organochemical inhibitors, such compounds may be identified in standard screening assays ... [o]nce identified, such an inhibitor may be used to inhibit NF-AT3 function in a therapeutic context."

In this regard, the examiner finds (Answer, page 8), the disclosed single chain antibody, cyclosporin A and FK506 "do not have any structural relationship with each other" let alone with the genus of molecules encompassed by appellants' claimed invention. The examiner finds (Answer, page 9),

> [t]he instant specification fails to provide sufficient descriptive information, such as definitive common structural features of the claimed NF-AT3 inhibitors. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. There is no description ... of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Furthermore, although molecular modeling is known in the art, the structure of the claimed mimetics or small molecule inhibitors is not known. The prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the encompassed NF-AT3 inhibitor molecules and no identifying characteristic or property of the instant NF-AT3 inhibitor molecules is provided such that one of skill would be able to predictably identify the encompassed NF-AT3 inhibitor molecules, as being identical to those instantly claimed.

"A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by

structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Lilly, provides the appropriate analysis. The claims in Lilly were directed generically to vertebrate or mammalian insulin cDNAs. See id. at 1567, 43 USPQ2d at 1405. The court held that a structural description of a rat cDNA was not an adequate description of these broader classes of cDNAs, because a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name, ' of the claimed subject matter sufficient to distinguish it from other materials." Id. (bracketed material in original).

The Lilly court explained that

> a generic statement such as. . . 'mammalian insulin cDNA,' without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus.

Id. at 1568, 43 USPQ2d at 1406. Finally, the Lilly court set out exemplary ways in which a genus of cDNAs could be described:

> A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.

Id.

Our appellate reviewing court revisited the issue of describing DNA. See Enzo Biochem, Inc. v. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court held that a claimed DNA could be described without, necessarily, disclosing its structure. The court adopted the standard that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.'" See id. at 1324, 63 USPQ2d at 1613 (emphasis omitted, ellipsis and bracketed material in original).

Post-Lilly, the court has clarified that the representative species need not necessarily be described in terms of their complete chemical structure. See Enzo Biochem, Inc. v. Gen-Probe Inc., 323 F.3d 956, 964, 63 USPQ2d 1609, 1613 (Fed. Cir. 2002) ("[T]he written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.'" (emphasis omitted, alterations in original)).

Our appellate review court has also noted that "Eli Lilly did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be

satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure." Amgen, Inc. v. Hoechst Marion Roussel, Inc., 314 F.3d 1313, 1332, 65 USPQ2d 1385, 1398 (Fed. Cir. 2003).

This standard applies to polypeptides as well as DNAs. See Rochester, F.3d at 925, 69 USPQ2d at 1893, "[w]e agree with Rochester that Fiers, Lilly, and Enzo differ from this case in that they all related to genetic material whereas this case does not, but we find that distinction to be unhelpful to Rochester's position. It is irrelevant; the statute applies to all types of inventions. We see no reason for the rule to be any different when non-genetic materials are at issue."

On this record, appellants claim a method for treating hypertrophy comprising the step of inhibiting, by any means, the function of NF-AT3 in a cardiomyocyte. While, appellants identify three agents that inhibit the function of NF-AT3, as discussed above, there is no evidence on this record that these agents are representative of the genus encompassed by the full scope of appellants' claimed invention, which includes a variety of structurally distinct agents.

We find that, with the exception of appellants' disclosure of (1) a single chain antibody antagonist of NF-AT3, (2) cyclosporin A, and (3) FK506, the specification does little more than describe the intended function of the inhibitors encompassed by the claimed method. There is no disclosed structural relationship among the genus of inhibitors encompassed by the claimed method. Simply put, the genus of inhibitors encompassed by the claimed method are

described only by their function.[5] For example, with reference to organochemical inhibitors, appellants' specification simply asserts (specification, page 28), "such compounds may be identified in standard screening assays." Appellants' specification, however, fails to provide any starting materials or common core structure that would inform a person of ordinary skill in the art as to where to begin a search for such inhibitors. Accordingly, we find no error in the examiner's rejection of claim 1 under the written description provision of 35 U.S.C. § 112, first paragraph.

For the foregoing reasons, we affirm the rejection of claim 1 under the written description provision of 35 U.S.C. § 112, first paragraph. As discussed supra, claims 4 and 9 fall together with claim 1.

Enablement:

Having disposed of all claims on appeal under the written description provision, we do not reach the merits of the rejection of the same claims under the enablement provision of 35 U.S.C. § 112, first paragraph.

Anticipation:

According to the examiner (Answer, page 17), "[t]here is no requirement in claim 1 that the treated cardiomyocyte is the cardiomyocyte of a subject having cardiac hypertrophy", therefore, "claim 1 does not recite a method of treating 'cardiac' hypertrophy." In addition, the examiner finds (id.), "claim 1 does not

[5] We find no evidence in the Gorczynski Declaration to the contrary.

require that the inhibition of NF-AT3 is by an agent that binds to and inactivates NF-AT3."

Based on the foregoing construction of appellants' claim 1, the examiner finds (Answer, pages 17-18), the administration of cyclosporin A, to treat either transplant coronary disease (Haverich), or cardiac transplantation (Reid), meet the requirements of claim 1. According to the examiner (Answer, page 18), although neither Haverich nor Reid "teach cardiomyocytes, it is well known in the art that the heart comprises cardiomyocytes, which are inherently exposed to cyclosporine A in the method of Haverich et al[.] or Reid et al." Relying on McCaffery and Martínez-Martínez as evidence, the examiner finds (id.), "cyclosporin A is an inhibitor of NF[-]AT3, and it is clear that the administered cyclosporin A taught by the art would inhibit the function of NF-AT3 in a cardiomyocyte."

As we understand the examiner's argument, appellants are simply claiming a new benefit of an old process. It is well-recognized that merely discovering and claiming a new benefit of an old process cannot render the process again patentable. In re Woodruff, 919 F.2d 1575, 1577-78, 16 USPQ2d 1934, 1936-37 (Fed. Cir. 1990); Verdegaal Bros., Inc. v. Union Oil Co., 814 F.2d at 632-33, 2 USPQ2d at 1054 ; Bird Provision Co. v. Owens Country Sausage, Inc. 568 F.2d 369, 375, 197 USPQ 134, 139 (5th Cir. 1978); In re Swinehart, 439 F.2d 210, 213, 169 USPQ 226, 229 (CCPA 1971); and Ex Parte Novitski, 26 USPQ2d 1389, 1391 (Bd. Pat. App. & Int. 1993). We note, however, as set forth in In re Oelrich, 666 F.2d 578, 581, 212 USPQ 323, 326 (CCPA

1981)(quoting Hansgirg v. Kemmer, 102 F.2d 212, 214, 40 USPQ 665, 667 (CCPA 1939)) (internal citations omitted):

> Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient. If, however, the disclosure is sufficient to show that the natural result flowing from the operation as taught would result in the performance of the questioned function, it seems to be well settled that the disclosure should be regarded as sufficient.

Therefore, as we understand it, the question before us is whether the prior art relied upon by the examiner is sufficient to establish that cyclosporin A is inherently treating hypertrophy as set forth in appellants' claimed invention.

To begin, we recognize that appellants do not dispute the examiner's interpretation of claim 1 as open to an agent that does not bind NF-AT3 directly, but instead inhibits the function of NF-AT3 indirectly. Accordingly, we find that appellants concede that claim 1 is open to agents that exert their effect on NF-AT3 indirectly, e.g., cyclosporin A.

We also recognize the dispute on this record as to whether claim 1 implicitly refers to "cardiac hypertrophy," or is open to include hypertrophy of a cardiomyocyte. According to appellants (Brief, page 12), "[t]he examiner appears to have misread the claims at issue, as the examiner asserts that the method is to treatment of a cardiomyocyte, when clearly claim 1 is directed to a method of treating cardiac hypertrophy." While appellants' specification does mention "cardiac hypertrophy"[6], the examiner points out there is no requirement in claim 1 that the method of treating hypertrophy be in a subject who has

[6] See e.g., Title of the Invention, "Methods and Compositions for Therapeutic Intervention in Cardiac Hypertrophy".

cardiac hypertrophy.[7] Answer, page 33. The examiner emphasizes, however, that she "did not assert that the claimed method is to treatment of [a] cardiomyocyte." Id.

We recognize the examiner's clarification of the rejection of record. Id. According to the examiner (id.), neither Haverich or Reid teach that hypertrophy can be treated with cyclosporin A. Nevertheless, the examiner asserts (Answer, bridging paragraph, pages 33-34), "since the art method steps are the same as the claimed method steps, i.e., inhibiting the function of NF-AT3, using the same claimed composition, i.e., in a cardiomyocyte, one would expect that inherently the method taught by the art would have the same effect as the claimed method."

In our opinion, the examiner's prima facie case of anticipation is missing one critical fact – a recognition in either Haverich or Reid that the patients receiving cyclosporin A had some form of hypertrophy that would be "inherently" treated with cyclosporin A. As appellants explain (Brief, page13), "[t]he prior art specifically deals with transplantation disease and cardiac function after transplant in response to CsA application. Transplantation disease has not and is not defined as cardiac hypertrophy, and it is possible to have one without the other, thus, there cannot be any inherency."

As discussed above, inherency may not be established by probabilities or possibilities. On this record, the examiner failed to establish that the cyclosporin

[7] In the event of further prosecution, we encourage the examiner and appellants to work together to clarify the language of claim 1. In this regard, we note appellants' assertion that claim 1 is "clearly" directed to "cardiac hypertrophy," accordingly, there should be no resistance to inserting the word "cardiac" before each occurrence of the word "hypertrophy" in appellants' claims.

A treated patients reported in either Haverich or Reid had some form of hypertrophy that would be "inherently" treated with cyclosporin A. In this regard, we remind the examiner that in order for a prior art reference to serve as an anticipatory reference, it must disclose every limitation of the claimed invention, either explicitly or inherently. See In re Schreiber, 128 F.3d 1473, 1477, 44 USPQ2d 1429, 1432 (Fed. Cir. 1997). Accordingly, it is our opinion that the examiner failed to meet her burden of establishing a prima facie case of anticipation. Therefore, we reverse the rejection of claim 1 under 35 U.S.C. § 102(b) as anticipated by any one of Haverich or Reid.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

Joan Ellis
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Donald E. Adams) APPEALS AND
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